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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/668,508	YOUNG ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-17 and 33-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-17 and 33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/2/07 has been entered.

Applicants' After-Final Amendment, filed 4/9/07, has been entered. Applicants have not filed an substantive remarks or arguments with the RCE request. The Examiner addresses Applicants' After-Final arguments, filed 4/9/07 in this Office action. Claims 14-17 are amended; claims 33-36 are newly added; claims 14-17, 33-36 are pending and under current examination.

Double Patenting

The prior rejection of claims 14-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 33 of copending Application No. 10/443,663 in view of Sambrook *et al.* is withdrawn in view of Applicants' arguments.

Claim Rejections - 35 USC § 112 – New Matter

The prior rejection of claims 14-17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter) is rendered moot in view of Applicants' amendment to the claims, which no longer recites "cannot give rise to functional gametes." However, a new rejection of record, necessitated by Applicants' amendment is found below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. This is a new ground of rejection necessitated by Applicants' amendment to the claims.

37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

The claims, as currently amendment, recite that the cells do not spontaneously different, remain quiescent in serum free medium and in the absence of an induction agent, and wherein the stem cell does not form tumors in an animal.

This is considered new matter because there is no description in the specification for a pluripotent embryonic-like stem cell that does not spontaneously differentiate, remains quiescent in serum free medium and in the absence of an induction agent, and does not form tumors in an animal. Particularly, Applicants have provided citations where it is asserted that support for this amendment can be found, however, these citations do not specifically provide support for these embodiments.

Applicants cite:

Pages 54-55 - which cite potential uses for the cells, but do not provide any specific guidance for the newly added embodiments.

Page 226, lines 11-14 – which recites that the cells remain quiescent in serum free media, however, this is directed to a PPMSC cell, which a pluripotent mesenchymal stem cell line. This stem cell line appears to be different than that which is instantly claimed, because the PPMSC cell line only forms tissues of

mesodermal lineage (p. 226, line 9), whereas the instant cells must be able to form cells derived from all of endodermal, ectodermal and mesodermal lineages.

Page 223, lines 17-21 – which lists a citation, but provides no guidance for the claim amendments.

Page 235, lines 6-9 - this citation is directed to pluripotent lineage-uncommitted mesenchymal stem cells. this appears to be the same cell line as that cited above as PPMSC, which are different than the cells instantly claimed. See also, above.

Examples 12-18 – these examples do not appear to provide specific support for the claim amendments. Applicants are invited, if they feel support if found in the as-filed disclosure, to point to this support, by page and line number.

Accordingly, the Examiner is unable to determine where support for the newly added limitations (does not spontaneously differentiate, remaining quiescent in serum free medium and in the absence of an induction agent, and does not form tumors in an animal) can be found in the as-filed disclosure; thus, these limitations is determined to introduce new matter into the as-filed disclosure.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 14-17 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP §2163.06 notes:

> *If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).*

MPEP §2163.02 teaches that:

> *Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in*

> *the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.*

MPEP §2163.06 further notes:

> *When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.* (Emphasis added).

Enablement

Claims 14-17 and newly added claims 33-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention. The claimed invention is directed to isolated pluripotent embryonic-like stem cells, derived from non-embryonic or postnatal animal cells or tissue, capable of self-renewal, differentiation to cells of each and any of endodermal, ectodermal and mesodermal lineages, wherein said pluripotent embryonic-like stem cells are not derived from embryonic tissue, are not totipotent

do not spontaneously differentiate, remaining quiescent in serum-free medium and in the absence of an induction agent, and wherein the stem cells do not form tumors in an animal, genetically engineered to express a gene or protein of interest.

Breadth of the claims. The claims broadly encompass isolated pluripotent embryonic-like stem cells from any species, isolated from any non-embryonic or postnatal animal cell or tissue.

Guidance of the Specification/The Existence of Working Examples. The specification teaches that an "embryonic-like pluripotent stem cell" is a cell that is capable of self-regeneration and differentiation of cells of endodermal, ectodermal and mesodermal lineages. See page 9, lines 5-11. The specification teaches that the pluripotent embryonic-like stem cells are isolated from various postnatal tissues and the cells were analyzed for differentiation capacity and expression of various markers. In particular, the specification teaches analysis of CF-NHDF2 (a dermis cell line), was incubated with dexamethasone and insulin for 45 days and examined morphologically, immunochemically and histochemically. See Example 9, p. 160. Additionally, the cell lines CM-SKM1 and CF-SkM2 were analyzed. The specification teaches that the cells were evaluated for alkaline phosphatase expression (indicating pluripotency), as well as extended capabilities for self-renewal, high levels of telomerase activity and induced differentiated cell types showing phenotypic markers for various tissue types. The specification further teaches that that these results indicate that the cells are pluripotent, embryonic-like stem cells. Tables 6-10 teach various markers that were tested, in particular, embryonic markers SSEA-1, SSEA-3, SSEA-4, H-CD34, H-CD66, and alkaline phosphatase were tested.

State of the Art/Predictability of the Art. The claims are directed to pluripotent embryonic-like stem cells, but the specification provides no specific guidance with regard to the cells and specific phenotypes such that one of skill in the art could, given the teachings of the specification, make and use these cells in

any of the contemplated uses. In particular, Table 7 recites various markers to show the differentiation capacity of the cells, however, the characterization of the cells as "embryonic-like" is not found to be predictable. In particular, the markers that are analyzed fail to uniquely identify embryonic stem cells, because these markers as expressed in other cell types. For example, the analysis in Table 7 reveals that the CF-NHDF2 cells express markers for embryonic carcinoma cells. Embryonic stem (ES) cells and embryonic carcinoma (EC) cells have fundamental, art-recognized differences. NIH: Stem Cells: Scientific Progress and Future Research Directions, Appendix C, June 2001 state that, "Human and EC cells differ in important ways. Human ES cells are euploid, meaning they carry the normal complement of chromosomes. In contrast, human EC cells are aneuploid; their chromosomes are distinctly abnormal. ... The ability of both cell types has been explored by injecting human ES and EC cells into immunocompromised mice. Injected human ES cells will form embryonic stem cell teratomas in mice, and the tumors consist of cells derived from all three germ layers. In contrast, human EC cell lines vary in their ability to differentiate in vivo but, in general are more limited than ES cells." See pages C-8 to C-9. Thus, the cells that the specification teaches expresses markers in EC cells, which are not expressed in ES cells, and further, EC cells are different than ES cells in various ways, including differentiation potential.

The specification teaches that the cells express alkaline phosphatase (see Table 7, for example). However, this particular marker fails to sufficiently and uniquely define an embryonic stem cell because it is expressed in other cell types. Alkaline phosphatase is a single marker that is expressed by pluripotent cells, however, the sole expression of this marker does not provide guidance that the cells are indeed ES cells. For example, Pera (J. of Cell Science, 113: 5-10, 2000) teaches that ES cells are identified by the presence of a repertoire of cell surface markers: SSEA-3,-4,TRA-1-60,TRA-1-81GCTM, as well as alkaline phosphatase (page 8,

Table 1). It is the collection of markers and not one alone that defines the pluripotent stem cell (page 9, col. 1, parag. 1, lines 6-22). None of these markers is completely taught by specification, and all of the markers can be detected in other tissue types (Pera, page 8, col. 1, parag. 1, line 1 to col. 2, line 1 and Eiges, page 135, col. 2, parag. 1, lines 13-14).). This repertoire of cell surface markers and alkaline phosphatase activity as a group is associated with the undifferentiated state of primate ES cells (Eiges, **FEBS Letters**, 529: 135-141 , 2002), page 135, col. 2, parag. 1, lines 1-7). Further, alkaline phosphatase activity is known to be present in human EBs, although it decreased as the EB ages. Embryoid bodies (EBs) are formed when ES cells differentiate (Gerecht-Nir, **Developmental Dynamics**, 232: 487-497 (2005), page 488, col. 1, lines 2-20). When ES cells are permitted to form EBs, alkaline phosphatase remains relatively the same before decreasing (see page 490, Table 1). Similarly, the specification teaches that the claimed cells express SSEA-4 (indicated by MC-813-70). See Table 7. Although SSEA-4 is a marker that is expressed in human ES cells, it is also expressed in mesenchymal stem cells; see Gang (**Blood**, 109(4): 1743-1751, February 15, 2007). Further, the NIH document (page C-8, Table C.1) shows that SSEA-4 is a marker expressed in monkey and human stem cells, but not in mouse embryonic stem cells. The claims are broadly directed to cells from <u>any species</u>, thus, there is no teaching, with regard to expression markers from cells other than human. Thus, although specification has shown that the pluripotent embryonic-like cells express alkaline phosphatase and SSEA-4, this does not provide sufficient guidance to show that these cells are "embryonic-like pluripotent stem cells", because theses markers do not specifically define and identify an ES cell, as shown by the above-cited art.

Additionally, Applicants have now added claims 33-36, which recites that the cells express SSEA4 and CD10, Applicants are referred to the prior Office action, which shows that pluripotent cells, such as ES cells, have specific characteristics, including differentiation potential, morphology, as well as specific cell markers,

which define these cells. SSEA-4 is a marker that is expressed in ES cells, as well as mesenchymal stem cells; further, the NIH document (cited above, page C-8, Table C.1) shows that SSEA-4 is a marker expressed in monkey and human stem cells, but not in mouse embryonic stem cells. The claims are broadly directed to cells from any species, thus, there is no teaching, with regard to expression markers from cells other than human. CD10 is a marker that is expressed in various cell types, including breast myoepithelial cells, leukemic cells in children, and various other cancer cells (see http://www.pathologyoutlines.com/cdmarkers.html#cd10, accessed online January 21, 2008, attached). Thus, Applicants' cells are no longer "embryonic-like stem cells" because they express markers and have phenotypes and characteristics that fail to establish that they are like an ES cell. Overall, the specification provides various markers that are expressed by the claimed cells, but does not provide sufficient guidance to show that these cells are "embryonic-like pluripotent stem cells", because theses markers do not specifically define and identify an ES cell, as shown by the above-cited art. Additionally, Applicants have amended the claims such that the cells do not form tumors in an animal. Given the art-recognized definition for an ES cell, which requires *in* vivo teratoma formation, Applicants' cells are no longer ES-like.

The Amount of Experimentation Necessary. Accordingly, in view of the lack of teachings or guidance provided by the specification, with regard to the identification and characterization of the claimed cells, the state of the art, which clearly shows that using particular markers fails to establish or uniquely identify ES cells, it would have required undue experimentation for one of ordinary skill in the art to make and use the claimed cells.

Written Description

Claims 14-17 and 33-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that, "[A]pplicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." *Vas-Cath Inc. v. Mahurkar,* 19USPQ2d at 1117. The specification does not, "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The specification teaches the analysis of various human cell lines that were isolated from postnatal tissues, and has determined that these cells are pluripotent, embryonic-like stem cells, based upon their ability to differentiate into various cell types, as well as markers expressed by the cells themselves. However, the specification fails to provide sufficient, identifying characteristics of the claimed cells such that one of skill in the art would recognize that Applicants had possession of the claimed cells. In particular, the markers used to identify the cells as "embryonic-like pluripotent stem cells" fail to be sufficiently described such that one of skill in the art could recognize and identify these cells. For example, Table 7 teaches differential expression markers of EC cells, and alkaline phosphatase, as well as SSEA-4 in conditions that include insulin and dexamethasone for the CF-NHDF2 cell line. Table 8 shows that the cells, after 37 doublings, do not express alkaline phosphatase, but at 40 doublings, express alkaline phosphatase, and after 45 doublings, no expression of alkaline phosphatase is noted. Cell line CM-SKM2 did not show any expression of alkaline phosphatase or SSEA-4 (Table 10). As shown above, these markers are expressed in ES cells, but not uniquely. Thus, it is unclear from Applicants' results what markers are expressed (or not) in the claimed cells, such that one of skill in the art could readily identify that Applicants had

possession of the claimed cells. Specifically, the specification fails to describe the markers and specific characterization of the cells (such as teratoma formation), and the skilled artisan, although recognizing that specific markers and characteristics identify pluripotent cells, could not envision which of such markers or characteristics, would uniquely identify Applicants' claimed cells.

See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification only provided the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description of 35 U.S.C. 112 is severable from its enablement provision [see p. 1115].

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14, 15 are unclear. The metes and bounds of the claims cannot be determined because it is unclear how Applicants' amendment further limits the claims.

1. The amendment in claim 14 (lines 4-5) that the cell is "not derived from embryonic tissue" is already present in lines 1-2 of the claim, which recite that the cell is derived from non-embryonic cells. Furthermore, the amendment recites

that the cell is "not totipotent", yet the claims are already limited to "pluripotent" cells. Pluripotent cells are not totipotent cells, they are not capable of producing extraembryonic tissues, and do not fulfill the definition of "totipotent". Thus, recitation that the cells are "not totipotent" does not limit the claim further.

2. Similarly, claim 15 part (a) recites that the cells are "derived from postnatal animal cells or tissue", yet Applicants' amendment recites that the "stem cells are not derived from embryonic tissue". This recitation is unclear, because the cells are limited to postnatal animal cells or tissue; therefore, embryonic tissues are not included in postnatal animals cells/tissue. Additionally, the amendment recites that the cell is "not totipotent", yet the claims are already limited to "pluripotent" cells. See above, #1.

Claims 16-17 depend from claim 15.

Claim Rejections - 35 USC § 102

The following rejections are withdrawn:

Claims 14-16 under 35 U.S.C. 102(b) as being anticipated by Capecchi.

Claims 14-16 under 35 U.S.C. 102(b) as being anticipated by Piedrahita

These rejections are withdrawn because Applicants have now amended to the claims to recite that the stem cell does not form tumors in an animal. The cells of Capecchi (mouse ES cells), and Piedrahita (porcine PGCs) form tumors upon injection into a host animal.

Claim Rejections - 35 USC § 103

The following rejections are withdrawn:

Claims 14-17 under 35 U.S.C. 103(a) as being unpatentable over Thomson when taken with Sambrook *et al.*

These rejections are withdrawn because Applicants have now amended to the claims to recite that the stem cell does not form tumors in an animal. The cells of Thomson (human ES) form tumors upon injection into a host animal.

Claims 14-17 stand rejected under 35 U.S.C. 103(a) being unpatentable over Shamblott when taken with Sambrook *et al.*

Applicants' arguments and amendments are not found to be persuasive. These amendments do not overcome the prior rejection of record, because the cells as taught by Shamblott fulfill the limitations of the claims. In particular, EG cells do not spontaneously differentiate – specific conditions must be provided in order to differentiate the cells. Additionally, all cells remain quiescent in serum-free media - this is a property of culturing cells in this type of media. Finally, the Examiner provides NIH, Chapter 3 of *Stem Cells: Scientific Progress and Future Research Directions.* Department of Health and Human Services. June 2001. <http://stemcells.nih.gov/info/scireport/2001report, to show that EG cells do not form tumors in an animal. See Table 3.1, page 15. Accordingly, because Applicants' amendment has not provided any discernable characteristics from the claimed cells and that of Shamblott, the prior rejection is maintained.

Shamblott *et al.* teach the generation of human pluripotent stem cells from gonadal ridges and mesenteries containing primordial germ cells [PGCs] and teach that embryoid bodies collected from these cultures revealed a wide variety of differentiated cell types, including derivatives of all three embryonic germ layers [see *Abstract*]. In particular, Shamblott *et al.* teach that gonadal ridges and mesenteries of 5 to 9 week old human fetuses and cells initially cultured on a layer of mouse STO fibroblast feeder layer. The cells formed embryoid bodies, which were collected and analyzed immunohistochemically [see pp. 13726-13727, *Materials & Methods*]. It was found that the embryoid bodies demonstrated derivatives of the three embryonic germ layers [see p. 13729, 2nd column and Table 1]. Note that

Shamblott teach the pluripotent embryonic-like stem cells because the claims do not provide any requisite characteristics (*e.g.*, specific markers, etc.) of the claimed embryonic-like stem cells such that they would be distinguished from the cells taught by Shamblott. The claims recite that the embryonic-like stem cells are "derived from non-embryonic or postnatal animal cells or tissue;" however, this recitation does not differentiate them from the cells as taught by Shamblott. Further, the method claim has been included in this rejection because the cells as instantly claimed are not distinguishable from those taught in the art. The cells as taught by Shamblott fulfill the requirements of the claims because they are capable of differentiation to cells of each and any of endodermal, ectodermal and mesodermal lineages, and are capable of self-renewal.

Shamblott do not teach the transfection of the pluripotent stem cells to produce a genetically engineered pluripotent stem cell. However, prior to the time of the claimed invention, Sambrook teach methods of transfecting mammalian cells with any gene of interest [see 16.33-16.38]. Accordingly, in view of the combined teachings of Shamblott and Sambrook, it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made, to use the PGCs, as taught by Shamblott and transfect them with any DNA of interest, with a reasonable expectation of success. One of skill in the art would have been sufficiently motivated to make such a modification, as expression of proteins in mammalian cells can provide different purposes, as described by Sambrook on p. 16.3, such as for the expression of large amounts of protein of biological interest, or to study the biosynthesis and intracellular transport of proteins following their expression in various cell types.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Peter Paras, SPE of Art Unit 1632, at (571) 272-4517. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Thaian N. Ton/
Primary Examiner
Art Unit 1632